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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/784,645	EMPEDOCLES ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-39 and 44-60* is/are pending in the application.

4a) Of the above claim(s) *27-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8 May 2003 has been entered.

Status of the Claims

2. Claims 1-26 and 40-43 are canceled. Claims 27-39 are withdrawn. New Claims 44-60 have been entered. The papers filed 8 May 2003 enters new Claims 44-57. The new claims incorrectly include two claims numbered 49, 50 and 56. New Claims 44-57 have been re-numbered according to 37 C.F.R. 1.126 as Claims 44-60.

The previous rejections in the Office Action dated 8 November 2002 are withdrawn in view of the amendments which cancel the rejected claims.

Claims 44-60 are under prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 45-51, 56 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 45-51 are indefinite in Claim 45 for the recitation "the tissue specimen" because the recitation lacks proper antecedent basis in the "tissue sections" of Claim 44. It is suggested that Claim 45 be amended to provide proper antecedent basis.

b. Claims 51, 56 and 57 are each indefinite because they depend from Claim 50. However, because the claim set contains two claims numbered 50, it is unclear from which Claims 51, 56 and 57 depend. For purposes of examination, the claims are interpreted as depending from the second Claim 50 which has been renumbered Claim 52.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 44-48, 50-51 and 54-55 are rejected under 35 U.S.C. 102(e) as being anticipated by Li et al (U.S. Patent No. 6,406,840, filed 17 December 1999) as defined by Bawandi et al (U.S. Patent No. 6,306,610 filed 17 September 1999).

Regarding Claim 44, Li et al disclose an analytical method comprising providing a tissue array comprising a plurality of tissue sections, contacting the array with a sample containing a first ligand which is linked to a label whereby the first ligand binds to a first antiligand of at least one tissue section to form a first complex, removing unbound ligand from the array and detecting and quantifying the presence of the complex wherein detection is an indication that the first complex contains the first antiligand (Column 22, line 15-Column 23, line 19). Li et al further teach the method wherein the label is a colloidal metal (Column 23, lines 4-9). Bawandi et al define semiconductor nanocrystals as colloidal metals (Column 12, lines 41-65). Therefore, the ligands of Li et al are linked to semiconductor nanocrystals as instantly claimed.

Regarding Claim 45, Li et al disclose the method wherein the plurality of tissue sections are located on a solid support at spatially encoded locations whereby the locations at which the first complex is formed provides an identify of the tissue at that location (Column 24, lines 15-60).

Regarding Claim 46, Li et al disclose the method wherein the plurality of tissues sections are from a single individual i.e. each tissue section represents a specific body tissue from an individual (Column 11, lines 31-34).

Regarding Claim 47, Li et al disclose the method wherein the plurality of tissue sections are from different individuals i.e. the "zoo array" wherein each sample represents a different organism and "personal cell array" comprising tissues from different family members (Column 11, lines 11-20 and Column 12, lines 3-8).

Regarding Claim 48, Li et al disclose the method wherein the plurality of sections are from the same type of tissue from each of the different individuals i.e. "personal cell array" comprising tissues from different family members (Column 12, lines 3-8).

Regarding Claim 50, Li et al disclose the method further comprising determining the location of the array the first complex is formed to identify tissue sections containing the first antiligand (Column 22, lines 15-29).

Regarding Claim 51, Li et al disclose the method wherein the plurality of tissues are from different types of tissues i.e. each tissue section represents a specific body tissue from an individual (Column 11, lines 31-34).

Regarding Claim 54, Li et al disclose the method wherein the first ligand is selected from the group consisting of antibodies, proteins, and nucleic acid probes (Column 7, lines 16-21 and 44-55).

Regarding Claim 55, Li et al disclose the method wherein the first antiligand is selected from the group consisting of proteins, and nucleic acids (Column 7, lines 16-21 and 44-55).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 44-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi et al (WO 99/44062, published 2 September 1999) in view of Bawandi et al (U.S. Patent No. 6,306,610, filed 17 September 1999).

Regarding Claim 44, Kallioniemi et al disclose an analytical method comprising providing a tissue array comprising a plurality of tissue sections, contacting the array with a sample containing a first ligand which is linked to a label whereby the first ligand binds to a

first antiligand of at least one tissue section to form a first complex, removing unbound ligand from the array and detecting and quantifying the presence of the complex wherein detection is an indication that the first complex contains the first antiligand (Example 5, page 25, line 30-page 28, line 2) wherein the label is fluorescent (page 25, lines 34-36) but they do not teach a semiconductor nanocrystal label. However, Bawandi et al teach a similar method for detecting a ligand wherein a ligand is contacted with an antiligand linked to a semiconductor nanocrystals (Column 22, lines 47-67)as colloidal metals (Column 12, lines 41-65). Bawandi et al further teach that semiconductor nanocrystal labels overcome known problems associated with known fluorescent labels and provide a broad range of excitation wavelengths, permit simultaneous detection of multiple distinct labels from a single source, they resist photobleaching (Column 4,lines 41-56). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace the fluorescent labels of Kallioniemi et al with the semiconductor nanocrystal labels of Bawandi et al. One of ordinary skill in the art would have been motivated to do so based on the teaching of Bawandi et al for the expected benefit of simultaneously detecting a plurality of non-degrading and distinct labels simultaneously using a single light source (Bawandi et al, Column 4,lines 41-56).

Regarding Claim 45, Kallioniemi et al disclose the method wherein the plurality of tissue sections are located on a solid support at spatially encoded locations whereby the locations at which the first complex is formed provides an identify of the tissue at that location (page 27, lines 13-25).

Regarding Claim 46, Kallioniemi et al disclose the method wherein the plurality of tissues sections are from a single individual i.e. multiple regions from a single tissue block (page 17, lines 8-10).

Regarding Claim 47, Kallioniemi et al disclose the method wherein the plurality of tissue sections are from different individuals i.e. 397 individual tumors (page 25,lines 32-34).

Regarding Claim 48, Kallioniemi et al disclose the method wherein the plurality of sections are from the same type of tissue from each of the different individuals e.g. breast cancer specimens (page 23, line 29-page 24, line 6).

Regarding Claim 49, Kallioniemi et al disclose the method wherein the different individuals share a common disease and the plurality of sections are from the same diseased tissue associated with the disease e.g. breast cancer specimens (page 23, line 29-page 24, line 6).

Regarding Claim 50, Kallioniemi et al disclose the method further comprising determining the location of the array the first complex is formed to identify tissue sections containing the first antiligand (page 27, lines 13-25).

Regarding Claim 51, Kallioniemi et al disclose the method wherein the plurality of tissue sections are from different individuals i.e. 397 individual tumors from differing sources (page 26, lines 13-24).

Regarding Claim 52, Kallioniemi et al disclose the method further comprising contacting the tissue with a labeled second ligand specific for an antiligand in the tissue i.e. CRBB2, MYC, CEP11, CEP17 and centromere-specific probes (page 26, lines 25-35)

Regarding Claim 53, Kallioniemi et al disclose the method wherein the tissue sections are from a plurality of different individuals and the method further comprises determining relative prevalence of binding between the first and second ligands i.e. comparison of gene-specific signals to centromere-specific signals (page 26, lines 32-35).

Regarding Claim 54, Kallioniemi et al disclose the method wherein the first ligand is selected from the group consisting of antibodies, proteins, and nucleic acid probes (page 4, lines 13-21 and 29-32).

Regarding Claim 55, Kallioniemi et al disclose the method wherein the first antiligand is selected from the group consisting of proteins, and nucleic acids (page 4, lines 13-21 and 29-32).

Regarding Claim 56, Kallioniemi et al do not teach the label is linked by a two-member binding pair. However, Bawandi et al teach their semiconductor nanocrystals linked to the first ligand via a linker comprising two member binding pair whereby a plurality of diverse antiligands are detected simultaneously (Column 22, lines 59-67). Bawandi et al teach their method wherein a plurality diverse antiligands are contacted with "disperate" anitligand-specific ligands, non-specific ligands are washed away and then antiligand-specific ligands are specifically and distinguishably linked to semiconductor nanocrystal labels (Column 22, lines 59-67). Bawandi et al further teach that this linking the semiconductor label utilizing this two-member binding pair technique (i.e. nanocrystal tags) simplifies multiplexing analysis utilizing known detection apparatus (Column 22, lines 32-46). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace the directly labeled ligands of Kallioniemi et al with the nanocrystal tag labeled ligands of Bawandi et al for the expected benefits of simplified multiplex analysis as taught b Bawandi et al (Column 22, lines 40-46).

Regarding Claims 57-58, Kallioniemi et al disclose the method wherein the first and second ligand are labeled prior to the contacting step (page 26, lines 25-35).

Regarding Claims 59-60, Kallioniemi et al disclose the method wherein the first and second ligand are labeled prior to the contacting step (page 26, lines 25-35) but do not teach that the ligands are labeled after the contacting step. However, Bawandi et al teach their method wherein the ligands are labeled after the contacting step utilizing nanocrystal tags. Bawandi et al further teach that labeling with the nanocrystal tags simplifies multiplexing analysis utilizing known detection apparatus (Column 22, lines 32-46). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace the directly labeled ligands of Kallioniemi et al with the nanocrystal tag labeled ligands of Bawandi et al for the expected benefits of simplified multiplex analysis as taught b Bawandi et al (Column 22, lines 40-46).

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 44-60 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,274,323 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods for detecting a target molecule by detecting fluorescence emitted by a semiconductor nanocrystal and differ only in the patent claims being drawn to the a single species of target molecule (i.e. polynucleotide) a single species of affinity moiety (i.e. PCR product) various species of first and second binding members (e.g. avidin and streptavidin, digoxygenin and anti-dioxygenin) while the instant claims are drawn to the genus ligand, anti-ligand and first and second binding pairs. The courts have stated that a genus is obvious in view of the teaching of a species (see; In re Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989) and MPEP 2131.02). Therefore, the instantly claimed methods

drawn to the genus target molecule and affinity moiety are obvious in view of the patent methods drawn to the species.

The sets of claims differ also in the that instant claims are drawn to detecting an anitligand in tissue sample on a tissue array while the '323 claims are drawn to detecting an anitligand in a sample. However, the '323 specification defines their "sample" via Example 17 as a tissue sample on a tissue array. Therefore, the "sample" recited in the patent claims encompasses the instantly claimed tissue sample.

11. Claims 44-60 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25, 27-29, 32, 35-39 and 53 of copending Application No. 09/887,914. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods comprising essentially the same steps differing only in the arrangement and grouping of the limitations i.e. immobilizing an anti-ligand, contacting the immobilized anti-ligand with a ligand linked to a semiconductor nanocrystal and detecting the semiconductor nanocrystal. The sets of claims differ only in the'914 claims are drawn to a species of ligand (i.e. polymerase chain reaction product) while the instant independent claims are broadly drawn to the genus ligand. The courts have stated that a genus is obvious in view of the teaching of a species (see Slayter, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989)). Therefore the instantly claimed ligand (i.e. genus) is obvious in view of the '914, polymerase chain reaction product (i.e. species).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
August 1, 2003